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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,903	07/11/2000	Heather J. Jordan	IVGN 187.1 CON	1446
65482	7590	09/06/2007	EXAMINER	
INVITROGEN CORPORATION			SISSON, BRADLEY L	
C/O INTELLEVATE				
P.O. BOX 52050			ART UNIT	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/613,903	JORDAN, HEATHER J.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 65-124, 126, 127, 130-133 and 135-139 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 65-124, 126, 127, 130-133 and 135-139 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 65-84 and 130-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 65 is indefinite with respect to what constitutes the metes and bounds of “substantially equal intensity.” A text search of the specification finds five instances of it being used, however, none of these instances has been found to provide a binding definition. Accordingly, the expression does not lend itself to ready determination of its metes and bounds.

4. Claims 130-133 recite limits of the “intensity,” however, the unit measure of the “intensity” is not clear. For example, is the “intensity” a function of a the strength of the light that is causing a fluorescence, or is it a function of the density of the stain that has been intercalated into the DNA (e.g., ethidium bromide), or is it a function of the total amount of label over the length of the nucleic acid fragment, or is it a function of some combination of the above-identified variables, or is it a function of some other variable? Furthermore, if some fragments are stained and some are not, but none of the fragments are subjected to UV light, then they would all have the same intensity.

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5. Hence, by claim 130 stipulating that the “intensity” is “no more than 3 times the intensity of any other fragment of said plurality,” claim 130 does not satisfy the requirements under 35 USC 112, second paragraph, as it is still unclear as to just what constitutes “intensity.”
6. Claims 131-133, like claim 130, as well as claims 66-84, which depend from claim 65, do not overcome this issue and are similarly rejected.

Response to argument

7. At pages 11 and 12 of the response received 02 July 2007, argument is presented as to what one of skill in the art would have understood the expression to mean. It is noted that the argument is unsupported by any evidentiary showing.
8. This argument has been fully considered and has not been found persuasive. Attention is directed to MPEP 2145.

Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) (“An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.”). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(f) he did not himself invent the subject matter sought to be patented.

10. Claims 65-82, 85-101, 103, 105-121, 123, and 130-133 are rejected under 35

U.S.C. 102(b) as being anticipated by US Patent 5,316,908 (Carlson et al.).

11. Carlson et al., Fig. 1, disclose a nucleic acid ladder that meets the size, relative mass, and intensity requirements of claims 65-82, 85-100, 105-120, and 130-133.

12. It is noted that claims 65, 85, and 105 are drawn to a nucleic acid ladder composition. The claims do not require that the ladder actually be part of any electrophoretic system or that they be stained, or even if they are stained, that the label be caused to fluoresce. Rather, the claims identify a range of fragment sizes. Accordingly, claims 80-82 do not further limit the nucleic acid ladder, but rather, provide additional means by which the comparison could be made.

13. It is noted with particularity that a compound and its properties are inseparable. While one may identify new properties or new means for evaluating same, such does not make an old compound, or old composition, new and patentable.

14. The claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art.

15. While Fig. 1 is a drawing and not a photograph, the specification does state that the Figure does represent the migration of the nucleic acid ladder in an electrophoretic environment. Said Figure clearly shows that the bands have the same relative intensity.

16. While argument is presented that the bands are not stained or caused to fluoresce, such argument is not persuasive, as claims 65-82, 85-100, 105-120, and 130-133 do not require such.

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Further, even if the claims were amended so to recite positive method steps, the claims are still drawn to a composition, not to a method.

17. While claims 81 and 82 recite detectable label to be used when performing the detection, however, the claims are not drawn to a method but to a product, which does not require the detectable label to be present.

18. To the extent that claims 103 and 123 do positively recite that the ladder is stained with ethidium bromide, it is noted that Carlson et al. disclose such, at column 4.

19. Claims 65-82, 85-101, 103, 105-121, 123, and 130-133 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. It is noted that the assignee of the '908 patent and the instant application at the time of filing are one and the same, yet the inventorship is different.

*Response to argument*

A review of the response of 02 July 2007 and 26 July 2007 fails to find where this rejection was specifically addressed. Therefore, and in the absence of convincing evidence to the contrary, the rejection is maintained.

***Claim Rejections - 35 USC § 103***

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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21. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. Claims 102 and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,316,908 (Carlson et al.) in view of Schneeberger et al.

23. See above for the basis of the rejection as it pertains to the disclosure of Carlson et al.

24. Carlson et al., discloses using a dye to stain the nucleic acid ladder but does not disclose using SYBR green.

25. Schneeberger et al., page 235, disclose that in conducting PCR, the formation of heteroduplexes can be eliminated by reducing the cycles of amplification from 30 to 25, but that this typically comes with a significant loss in sensitivity. Schneeberger et al., go on to teach that “sensitivity can be restored by using a novel and extremely sensitive DNA stain,” which is SYBR Green. Schneeberger et al., page 235, right column, teach that SYBR Green is five times as sensitive as ethidium bromide.

26. In view of the teachings of the prior art, one would have been motivated to have modified the nucleic acid ladder of Carlson et al., by staining same with SYBR green as disclosed by Schneeberger et al., as such is explicitly disclosed as being extremely sensitive stain which can be used in place of ethidium bromide. As disclosed by Schneeberger et al., when conducting

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PCR and running the amplicons on a gel, increased sensitivity is achieved by using SYBR green, which in turns allows for fewer rounds of amplification and the artifact associated therewith.

27. In view of the detailed teachings, said ordinary artisan would have been highly motivated and would have also had a most reasonable expectation of success.

28. Claims 126, 127, and 135-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,316,908 (Carlson et al.).

29. See above for the basis of the rejection as it pertains to the disclosure of Carlson et al.

30. Carlson et al., disclose nucleic acid ladders that comprise numerous bands that span a wide range of fragment sizes. While some of the rungs of the nucleic acid ladder fall within the recited ranges of claims 126, 127, and 135-139, the disclose nucleic acid ladders also comprise additional nucleic acid fragments that are outside of the recited range.

31. The selection of which band or combination of bands, and their relationship to one another is not deemed to constitute a patentable distinction over the prior art. Rather, such limitations are deemed to be the result of design choice and/or routine optimization.

32. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In *re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In *re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In *re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In *re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility



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over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmischer, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

Attention is directed to the decision in KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)

[T]he appeals court erred in assuming that a person of ordinary skill in the art attempting to solve a problem will be led only to those prior art elements designed to solve the same problem. ... It is common sense that familiar items may have obvious uses beyond their primary purposes, and a person of ordinary skill often will be able to fit the teachings of multiple patents together like pieces of a puzzle... Third, the court erred in concluding that a patent claim cannot be proved obvious merely by showing that the combination of elements was obvious to try. When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. Finally, the court drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. Rigid preventative rules that deny recourse to common sense are neither necessary under, nor consistent with, this Court's case law.

33. In the present case, applicant is claiming ladders of nucleic acid fragments that range in size. The prior art clearly discloses such ladders and ranges of size. While the prior art may not explicitly recite the mass relationships now found in the rejected claims, such is deemed to be obvious in view of the prior art.

34. For the above reasons, and in the absence of convincing evidence to the contrary, claims 126, 127, and 135-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,316,908 (Carlson et al.).

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35. Claims 83, 84, 104, and 124 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,316,908 (Carlson et al.) in view of US Patent 5,527,670 (Stanley).

36. See above for the basis of the rejection as it relates to the disclosure of Carlson et al.

37. Carlson et al., while teaching of the staining of a gel through the use of a dye, and of conducting gel electrophoresis, has not been found to disclose the addition of a dye such as bromophenol blue.

38. Stanley, column 10, second paragraph, discloses the addition of a loading dye, which comprises bromophenol blue, to a mixture of oligonucleotides that are to be separated via gel electrophoresis.

39. It would have been obvious to one of ordinary skill in the art to have incorporated the use of a dye such as bromophenol blue, into the nucleic acid ladder composition of Carlson et al., as such would have facilitated the ready identification of the sample having been loaded into the gel and of its migration into the gel matrix. In view of the well-developed nature of gel electrophoresis, said artisan would have had a most reasonable expectation of success.

40. For the above reasons, and in the absence of convincing evidence to the contrary, claims 83, 84, 104, and 124 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,316,908 (Carlson et al.) in view of US Patent 5,527,670 (Stanley).

Response to argument

Argument is presented at page 13 of the response received 02 July 2007 that the rejection of claims under 35 USC 103(a) should be withdrawn as Carlson et al., does not disclose thee

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claimed invention. As shown above, however, the publication of Carlson et al. is deemed to disclose the claimed invention and as such, the rejection is maintained.

### ***Conclusion***

41. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

42. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

43. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

44. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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45. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/  
Primary Examiner  
Art Unit 1634

BLS